Approach to the Cyanotic Newborn

Satyan Lakshminrusimha
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Topics covered today
- What is cyanosis?
- Fetal Circulation
- Causes of cyanosis
- Some case descriptions and errors in diagnosis
- Cardiac, Respiratory and Hematologic causes
- Differentiating respiratory from cardiac cyanosis

Cyanosis
- Slatey blue discoloration of mucous membranes, skin and nail beds
- Skin pigmentation, observer’s acuity, hemoglobin concentration
- More accurate and sensitive measurement now with the use of pulse oximetry

Differential Cyanosis
- Upper normal – lower hypoxic
  - Pulmonary Hypertension (Persistent Fetal circulation)
  - Co-A, PDA
  - Interrupted aortic arch
- Upper hypoxic – lower normal
  - TGA, Co-A with PDA

Differential Cyanosis
- Periphery hypoxic – central normal
  - Acrocyanosis
  - Relatively slow flow of blood through an area with a resultant large arterio-venous oxygen difference
  - Hands, feet and circumoral area are common sites

Normal Fetus
Fetus is Normally Cyanotic!

Arrows indicate sites of arterio-venous shunts in the placenta.

Case # 1

- 28 year old G1P0 diabetic mother with good prenatal care delivers a 39 week AGA baby by C-section
- At 5 min of age baby is cyanotic, with good respiratory effort with a pulse ox – 80%

Pulse Oximeter Use in the Delivery Room

- Apply sensor to the baby first
- Then connect the sensor to the pulse oximeter
- Turn on the pulse oximeter
- Time to display oxygen saturation 68 (58-90) sec from birth
- If sensor is applied to the baby last – 100 (74-150 sec)

Normal Newborn Infant is Cyanotic!

Kaplan-Meier curves showing the percentage of infants reaching an SpO2 ≥ 85% over time (minutes)


Causes of Cyanosis

CARDIAC – 5 Ts
- Transposition of great vessels (TGA)
- Tetrology of Fallot
- Truncus arteriosus
- Tricuspid Atresia
- Total Anomalous Pulmonary Venous Circulation
- Single ventricle morphology
- Ebstein’s anomaly

RESPIRATORY
- Transient Tachypnea of Newborn (Malignant)
- Aspiration syndrome (Meconium, amniotic fluid, blood...)
- Congenital Diaphragmatic Hernia (CDH) / Choanal atresia
- Hyaline membrane disease
- Pneumonia / sepsis
- Nubain – maternal analgesia
- Esophageal atresia
- Air-leak syndromes (Pneumothorax)
- Persistent Pulmonary Hypertension of Newborn

HEMATOLOGIC – Polycythemia, Methemoglobinemia, Hb M

Case # 2 – 2 day old with cyanosis

Baby G was born by SVD after a normal uneventful pregnancy with good prenatal care
- Baby weighed 8 lbs 8 oz with Apgar scores 7 (1) and 8 (5) and had a normal newborn exam
- On 2nd day of life, before being sent home the nurse thinks his hands look dusky and checks pulse ox – it is 78%

Examination

- No obvious cyanosis
- No heart murmur
- Pulse ox is in the 70s with good peripheral pulses
- ABG done in room air – 7.37 / 32 / 35 / -4, Hgb - 14 g/dL
- A chest X-ray is obtained
- Baby is placed on 90% oxygen resulting in no clinical improvement, ABG – 7.34/34/52/-5

Basis of Hyperoxia Test

Large amount of oxygen chemically combines with hemoglobin

<table>
<thead>
<tr>
<th>PO2 (torr)</th>
<th>SO2 (%)</th>
<th>O2 Combined with Hb (ml/100ml)</th>
<th>O2 dissolved in plasma (ml/100ml)</th>
<th>Total O2 content per 100ml of blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td>60</td>
<td>12.0</td>
<td>0.1</td>
<td>12.1</td>
</tr>
<tr>
<td>100</td>
<td>100</td>
<td>20.1</td>
<td>0.3</td>
<td>20.4</td>
</tr>
<tr>
<td>600</td>
<td>100</td>
<td>20.1</td>
<td>3.8</td>
<td>21.9</td>
</tr>
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Hemoglobin (Hb) concentration in this case < 15 g / 100 ml
Each gram of Hb when fully saturated, combines with 1.34 ml of oxygen
Dissolved oxygen is usually 0.3 ml in 100 ml for each 100 mmHg

Oxygen Content of Blood at Different Levels of Oxygen Tension

Basis of Hyperoxia Test

- Oxygen content of blood has a direct relationship with oxygen saturation (and not oxygen tension)

<table>
<thead>
<tr>
<th>Volume of Blood</th>
<th>PaO₂ (mmHg)</th>
<th>% Saturation</th>
<th>Dissolved O₂ (ml/dL)</th>
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<tr>
<td>50 ml</td>
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</tr>
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<td>60%</td>
<td>21.9 ml</td>
</tr>
<tr>
<td>100 ml</td>
<td>45</td>
<td>80%</td>
<td>17 ml</td>
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Oxygen-Hemoglobin Dissociation Curve

Hyperoxia Test and Cyanosis

- Normal response
  - PaO₂ = 80 on 21%
  - Pulmonary disease
    - PaO₂ = 45 on 21%
  - TGV or ductal dependant PBF
    - PaO₂ = 30 on 21%
  - Admixture lesions*
    - PaO₂ = 40 on 21%

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Transposition of Great Arteries

- Common cause of CHD with cyanosis in the first week of life – 5% of CHD
- Good looking neonates with normal to slightly high birth weight
- Usually have good prenatal care but occasionally not diagnosed antenatally

Why was this diagnosis missed on prenatal ultrasound?

~ 83-85% of CHD are picked up on antenatal sonograms
Fetal Echocardiography
- Four-chamber view
- Great arteries and pulmonary veins are difficult to assess
- TGA, Coarctation and isolated TAPVR often missed without a specialized fetal sonogram / echocardiogram

TGA
- Presents with severe cyanosis (pO₂ 20-30’s or O₂ sats 50-70’s) in the 1st week. Newborns with TGV and VSD or ASD are less cyanotic
- Frequently have no murmur
- Loud single S2 because of anterior aorta
- "Egg shaped heart" on CXR in 1/3 of patients

Why was a neonate with PaO₂ of 35 mmHg missed on newborn exam?
- Variable Hgb in newborn
- Experience of the observer
  - Often first noticed by an experienced nurse
- Presence of Hemoglobin F (fetal)
- Presence of ductus arteriosus
- Presence of patent foramen ovale

Variable Hemoglobin in Newborn
- Clinical cyanosis results from the presence of 5 g/dL of unsaturated hemoglobin in the systemic circulation
- The presence of cyanosis depends on Hgb concentration
- Hgb concentration in term newborn can vary from 13.7 to 20.1 g/dL

Term Newborn – 70% Fetal Hb
- Oxygen Saturation mentioned on blood gas may be misleading

An Open Ductus can Sustain Life in Many CHDs
- Left sided lesions
  - Coarctation of Aorta
  - Critical Aortic Stenosis
- Hypoplastic left heart syndromes
- Mixing Lesions
  - Transposition
- Right sided lesions
  - Tricuspid atresia
  - Severe pulm stenosis

Fetal Circulation with TGA
Immediate Management

- Arrange for transfer to a center with surgical services
- Maintain Oxygen saturation in high 70s and low 80s
- Fluid & Electrolyte Management
- Place Umbilical Venous and Arterial lines
- Start Prostaglandin E1

Prostaglandin E1 (Alprostadil)

- Prostin VR Pediatric: 500 mcg/ml (1 ml)
- Usual starting dose (0.05 mcg/kg/min to 0.1mcg/kg/min)
- Maintenance may be as low as 0.01 mcg/kg/min
  - Prefer lower starting dose (0.025 mcg/kg/min) to avoid side effects
  - Immediate Apnea* – 10 to 12%, dose-dependent, occurs in the first hour of infusion (i.e., before the transport team arrives if you are in a community hospital)
  - Fever
  - Long-term – cortical hyperostosis, pyloric stenosis
  - Causes Pulmonary vasodilation (beneficial in PPHN also)

* Can be treated or prevented with aminophylline

Prostaglandin E1 - Order

- Use sheets provided by Pharmacy
- If sheets are not available (especially in a community hospital):
  - Mix 500 mcg of Prostin in 50 ml of Normal Saline
  - Infusion Rate (0.3 X Weight in Kg) in cc per hour
  - Provides 0.05 mcg/kg/min
  - Example:
    - 3 kg infant – 0.9 cc/hr

Avoid concentrations higher than 20 mcg/ml (high osmolality)

Prostaglandin E1 – Alternate Route of Administration – very high UAC

TGA – Rashkind’s Procedure

- Superior vena cava
- Inferior vena cava
- Pulmonary veins
- LA
- LV
- TA
- Pulmonary Artery
- RA
- RV
- Aorta
- Patent Ductus
Neonatal X-rays

Seven Dwarfs
- Hazy - RDS
- Grainy - RDS
- Patchy - pneumonia
- Streaky - TTN
- Fluffy - MAS
- Bubbly - PIE
- Blacky - Idiopathic PPHN

Snow – Whitey – TAPVR (cardiac)

Cyanosis in the Newborn Infant

Low PaO₂, SaO₂

<table>
<thead>
<tr>
<th>Cardiac</th>
<th>Pulmonary or Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased cyanosis</td>
<td>Crying</td>
</tr>
<tr>
<td>Tachypnea, slow, deep</td>
<td>Respiratory distress</td>
</tr>
<tr>
<td>Normal or decreased</td>
<td>FiCO₂</td>
</tr>
<tr>
<td>Minimal response</td>
<td>FiO₂</td>
</tr>
<tr>
<td>Murmur, weak pulses</td>
<td>Cardiac exam</td>
</tr>
<tr>
<td>Can be abnormal</td>
<td>EKG</td>
</tr>
<tr>
<td>Abnormal</td>
<td>ECHO</td>
</tr>
<tr>
<td>Heart abnormal or normal</td>
<td>Chest X-ray</td>
</tr>
<tr>
<td>Abnormal pulmonary blood flow</td>
<td></td>
</tr>
</tbody>
</table>

Case # 3

3.5 kg
38 week gestation
Emergency C-section for fetal distress due to abruption
Bag-mask ventilation Apgar 8 (1) / 8 (5)

EKG – Abnormal Northwest Axis

Neonate with superior axis
In failure (Endocardial cushion defect)
Cyanotic (Tricuspid Atresia)

Respiratory Cyanosis

- Anxiety
- Tachypnea (increased resp. rate)
- Hyperpnea (increased depth – normal tidal volume is 4-6 ml/kg)
- Tachycardia

Nasal Flaring
Use of accessory muscles
Retractions
May compensate and maintain oxygenation & ventilation

Normal mean respiratory rates: NB – 40 (<60)

Cyanotic Baby Girl

- Pulse oximeter
- Predial: 88%
- Postdial: 78%
- Intubated
- Mechanical ventilation
- Clear lung fields
- Significant improvement in PaO₂ transiently but deteriorated rapidly
- Transient response to hyperventilation
- No improvement with surfactant and HFOV
Echocardiogram Case # 3

- R → L shunt
- Extrapulmonary shunting
  - PFO
  - Ductus arteriosus
  - Tricuspid regurgitation
- Good cardiac function
  - On low doses of dopamine and dobutamine
- Clear Chest X-ray
- Diagnosis
- Management?

Persistent Pulmonary Hypertension of the Newborn (PPHN)

Primary Respiratory with pulmonary vascular Etiology for Cyanosis

PPHN

PPHN is a syndrome characterized by high pulmonary vascular resistance (PVR) causing extrapulmonary right-to-left shunting of blood across the ductus arteriosus and/or foramen ovale.

Cardio-pulmonary interactions in PPHN

Muscularization of alveolar capillaries

Increased Muscularization of pulmonary arterioles

Effect of inhaled NO

Nitric Oxide Gas

NO

Selective pulmonary vasodilation

Legion to Hb

Lack of NO leads to vasoconstriction

Micro-selective effect decreases intrapulmonary shunting
Course

- Baby had an initial response with improvement in oxygenation with 20 ppm of inhaled NO
- Six hours later there was deterioration in oxygenation

Phosphodiesterase Inhibitors

- Dipyridamole – PDE 5
- Milrinone – PDE 3
- Caffeine/Theophylline – PDE 1
- Sildenafil (Viagra)
- Newer PDE 5 inhibitors
  - Levitra
  - Cialis

Nitric Oxide – Non-responder

- NO - Nonresponder + Sildenafil

The use of sildenafil for treatment of PPHN is not approved in pediatric age group
Use of Sildenafil in PPHN

- Intravenous form under investigation (not currently available)*
- Oral suspension (formulated by pharmacist) at 2mg/kg
- Tablets (Viagra – 50 mg, Revatio – 20 mg)
- Dose – 0.3 to 1 mg/kg per dose OG/PO q 6-12 h (some case reports – 2mg/kg/dose)
- Experimental – use with caution
- Risk of visual disturbances (and ROP)


Oral Sildenafil in Severe PPHN

- Oral Sildenafil in Infants With Persistent Pulmonary Hypertension of the Newborn: A Pilot Randomized Blinded Study PEDIATRICS Vol. 117 No. 4 April 2006, pp. 1077-1083
- Survival 6/7 – sildenafil; 1/6 – placebo; No change in systemic blood pressure

Case # 4 – Term infant in newborn nursery with tachypnea, respiratory distress and hypoxia

- Born to a GBS + mother
- Inadequate intrapartum antibiotic prophylaxis
- Onset of tachypnea at 36 h of life

Physical Examination

- Tachypneic infant with mild retractions (RR-85/min)
- Pulse oximeter low 80s in room air and low 90s on 9 LPM mask oxygen
- Initial diagnosis of GBS sepsis with PPHN
- Blood gas (ABG) from newborn nursery: 7.42/35/42/-0.2 on oxygen
- Started on Ampicillin and Gentamicin
- Baby transferred to NICU and chest X-ray obtained

Echocardiogram

- Baby was initially placed on nasal CPAP and then on mechanical ventilation
- Right to left shunt at the PFO
- Dilated RV and main PA
- No tricuspid regurgitation
- CBC – No left shift
- No metabolic acidosis
PPHN
- Arterial oxygenation unchanged despite mechanical ventilation with ~ 100% oxygen
- Inhaled Nitric oxide given at 20 ppm for one hour
- No change in oxygenation (PaO₂ – 44 mmHg on inhaled NO)
- Inhaled NO discontinued
- No respiratory or metabolic acidosis
- Repeat echocardiogram – no change in findings

Total Anomalous Pulmonary Venous Connections
- 1% of congenital heart disease
- Classified: supracardiac (SVC, innominate v)
  cardiac (RA, coronary sinus)
  infracardiac (subdiaphragmatic)
- If unobstructed presents with mild to moderate cyanosis and CHF at weeks to months
- If obstructed (infracardiac) presents early with severe cyanosis
- May be associated with asplenia syndrome

Snowman in a Snowstorm
Appearance
**Infradiaphragmatic TAPVR** – Often mistaken for a Respiratory Condition

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**One day old term newborn**

**Hypoxia Hypotension**

- Born at a peripheral community hospital
- One day old term newborn male
- Uneventful prenatal course and delivery
- Noted to have poor perfusion – pulse oximeter 78% in room air
- Placed in 100% oxygen, one normal saline bolus administered
- Transport initiated – intubated for transport
- Baby was in shock on arrival at the referral center

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**Hypoplastic Left Heart / single Ventricle physiology lesions**

- Common Pumping Chamber
- Lungs
- Pulmonary Artery
- Ductus
- Aorta

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**The Treatment for Cyanosis is not always Oxygen**

- To give or not to give OXYGEN is the question
- In Respiratory Disorders & Pulmonary Hypertension, Oxygen...
  - Relieves hypoxia
  - Pulmonary vasodilator
  - Watch for oxygen toxicity
- In Ductal Dependent Cardiac Disorders, Oxygen...
  - Closes the ductus
  - Reduces Systemic Circulation

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**Excessive Oxygen Administration**

- Common Pumping Chamber
- Lungs
- Pulmonary Vasodilation
- Ductal Constriction
- Aorta
- Ischemia
- Anuria
- Acidosis
- Gut necrosis
- Seizures